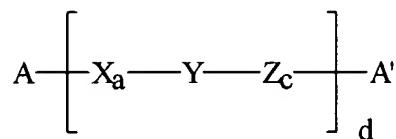


IN THE CLAIMS

Please delete all prior lists of claims in the application and insert the following list of claims:

1-3. (CANCELED)

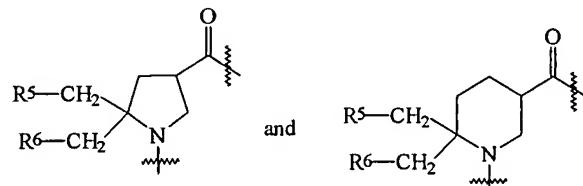
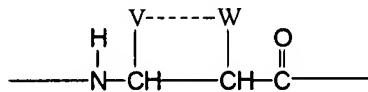
4. (CURRENTLY AMENDED) An isolated, unnatural polypeptide compound of formula:

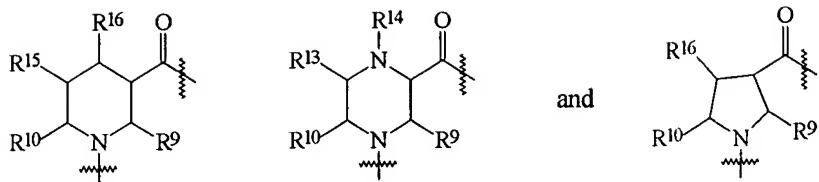


wherein:

each X and each Z is independently variable and is selected from the group consisting of α -amino acid residues, β -amino acid residues, and γ -amino acid residues, provided that at least one X or Z ~~comprises is~~ an α -amino acid residue and at least another two of X or Z ~~comprise are~~ two cyclically-constrained β -amino acid residues; and

wherein each cyclically-constrained β -amino acid residue is independently selected from the group consisting of:





wherein V and W are combined, together with the carbon atoms to which they are bonded, and independently define a substituted or unsubstituted, monocyclic or bicyclic C₃-C₁₀ cycloalkyl, cycloalkenyl or heterocyclic ring having one or more N, O or S atom(s) as the heteroatom(s);

the substituents on carbon atoms of the rings being independently selected from the group consisting of linear, branched, or cyclic C₁-C₆-alkyl, alkenyl, alkynyl; mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl-C₁-C₆-alkyl, and mono- or bicyclic heteroaryl-C₁-C₆-alkyl, ~~and the substituents listed above for V and W;~~

the substituents on nitrogen heteroatoms of the rings being independently selected from the group consisting of hydrogen, monocyclic or bicyclic C₁-C₁₀-alkyl, alkenyl, or alkynyl; mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl-C₁-C₆-alkyl, mono- or bicyclic heteroaryl-C₁-C₆-alkyl, -S(=O)₂-R¹⁷, -C(=O)-R¹⁷, -S(=O)₂-(CH₂)_{n+1}-R¹⁸, and -C(=O)-(CH₂)_n-R¹⁸, where n = 1 to 6;

wherein R¹⁷ is independently selected from the group consisting of hydrogen, monocyclic or bicyclic C₁-C₁₀-alkyl, alkenyl, or alkynyl; mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl-C₁-C₆-alkyl, mono- or bicyclic heteroaryl-C₁-C₆-alkyl; and

wherein R¹⁸ is independently selected from the group consisting of hydroxy, linear, branched, or cyclic C₁-C₆-alkyl, alkenyl, or alkynyl; mono- or bicyclic aryl,

mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl-C₁-C₆-alkyl; mono- or bicyclic heteroaryl-C₁-C₆-alkyl; C₁-C₆-alkyloxy, aryloxy, heteroaryloxy, thio, C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, arylthio, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroaryl sulfinyl, heteroarylsulfonyl, amino, mono- or di-C₁-C₆-alkylamino, mono- or diarylamino, mono- or diheteroaryl amino, N-alkyl-N-aryl amino, N-alkyl-N-heteroaryl amino, N-aryl-N-heteroaryl amino, aryl-C₁-C₆-alkylamino, carboxylic acid, carboxamide, mono- or di-C₁-C₆-alkylcarboxamide, mono- or diarylcarboxamide, mono- or diheteroarylcarboxamide, N-alkyl-N-arylcarboxamide, N-alkyl-N-heteroarylcarboxamide, N-aryl-N-heteroarylcarboxamide, sulfonic acid, sulfonamide, mono- or di-C₁-C₆-alkylsulfonamide, mono- or diarylsulfonamide, mono- or diheteroarylsulfonamide, N-alkyl-N-arylsulfonamide, N-alkyl-N-heteroarylsulfonamide, N-aryl-N-heteroarylsulfonamide, urea; mono- di- or tri-substituted urea, wherein the substituent(s) is selected from the group consisting of C₁-C₆-alkyl, aryl, heteroaryl; O-alkylurethane, O-arylurethane, and O-heteroarylurethane; and wherein R⁵ and R⁶ are independently selected from the group consisting of hydrogen, hydroxy, linear, branched, or cyclic C₁-C₁₆-alkyl, alkenyl, or alkynyl; mono- or di- C₁-C₁₆ alkylamino; mono- or bicyclic aryl; mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl-C₁-C₁₆-alkyl; mono- or bicyclic heteroaryl-C₁-C₁₆-alkyl; -(CH₂)₀₋₆-OR⁷, -(CH₂)₀₋₆-SR⁷, -(CH₂)₀₋₆-S(=O)-CH₂-R⁷, -(CH₂)₀₋₆-S(=O)₂-CH₂-R⁷, -(CH₂)₀₋₆-NR⁷R⁷, -(CH₂)₀₋₆-NHC(=O)R⁷, -(CH₂)₀₋₆-NHS(=O)₂-CH₂-R⁷, -(CH₂)₀₋₆-C(=O)-OH, -(CH₂)₀₋₆-C(=O)-OR⁷, -(CH₂)₀₋₆-C(=O)-NH₂, -(CH₂)₀₋₆-C(=O)-NHR⁷, -(CH₂)₀₋₆-C(=O)-N(R⁷)₂, -(CH₂)₀₋₆-O-(CH₂)₂₋₆-R⁸, -(CH₂)₀₋₆-S-(CH₂)₂₋₆-R⁸, -(CH₂)₀₋₆-S(=O)-(CH₂)₂₋₆-R⁸, -(CH₂)₀₋₆-S(=O)₂-(CH₂)₂₋₆-R⁸, -(CH₂)₀₋₆-NH-(CH₂)₂₋₆-R⁸, -(CH₂)₀₋₆-N-{(CH₂)₂₋₆-R⁸}₂, -(CH₂)₀₋₆-NHC(=O)-(CH₂)₂₋₆-R⁸, and -(CH₂)₀₋₆-NHS(=O)₂-(CH₂)₂₋₆-R⁸; wherein

R^7 is independently selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, alkenyl, or alkynyl; mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl- C_1 - C_6 -alkyl, mono- or bicyclic heteroaryl- C_1 - C_6 -alkyl; and

R^8 is selected from the group consisting of hydroxy, C_1 - C_6 -alkyloxy, aryloxy, heteroaryloxy, thio, C_1 - C_6 -alkylthio, C_1 - C_6 -alkylsulfinyl, C_1 - C_6 -alkylsulfonyl, arylthio, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, amino, mono- or di- C_1 - C_6 -alkylamino, mono- or diarylamino, mono- or diheteroaryl amino, N-alkyl-N-aryl amino, N-alkyl-N-heteroaryl amino, N-aryl-N-heteroaryl amino, aryl- C_1 - C_6 -alkylamino, carboxylic acid, carboxamide, mono- or di- C_1 - C_6 -alkylcarboxamide, mono- or diarylcarboxamide, mono- or diheteroarylcarboxamide, N-alkyl-N-arylcarboxamide, N-alkyl-N-heteroarylcarboxamide, N-aryl-N-heteroarylcarboxamide, sulfonic acid, sulfonamide, mono- or di- C_1 - C_6 -alkylsulfonamide, mono- or diarylsulfonamide, mono- or diheteroarylsulfonamide, N-alkyl-N-arylsulfonamide, N-alkyl-N-heteroarylsulfonamide, N-aryl-N-heteroarylsulfonamide, urea; mono- di- or tri-substituted urea, wherein the substituent(s) is selected from the group consisting of C_1 - C_6 -alkyl, aryl, heteroaryl; O-alkylurethane, O-arylurethane, and O-heteroarylurethane; and

wherein R^9 is selected from the group consisting of linear, branched, or cyclic C_1 - C_6 -alkyl, alkenyl, or alkynyl; mono- or di- C_1 - C_6 alkylamino, mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl- C_1 - C_6 -alkyl, mono- or bicyclic heteroaryl- C_1 - C_6 -alkyl, $-(CH_2)_{1-6}-OR^{11}$, $-(CH_2)_{1-6}-SR^{11}$, $-(CH_2)_{1-6}-S(=O)-CH_2-R^{11}$, $-(CH_2)_{1-6}-S(=O)_2-CH_2-R^{11}$, $-(CH_2)_{1-6}-NR^{11}R^{11}$, $-(CH_2)_{1-6}-NHC(=O)R^{11}$, $-(CH_2)_{1-6}-NHS(=O)-CH_2-R^{11}$, $-(CH_2)_{0-6}-C(=O)-OH$, $-(CH_2)_{0-6}-C(=O)-OR^{11}$, $-(CH_2)_{0-6}-C(=O)-NH_2$, $-(CH_2)_{0-6}-C(=O)-NHR^{11}$, $-(CH_2)_{0-6}-C(=O)-N(R^{11})_2$, $-(CH_2)_{1-6}-O-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-S-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-S(=O)-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-S(=O)_2-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-NH-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-N-\{(CH_2)_{2-6}-R^{12}\}_2$, $-(CH_2)_{1-6}-NHC(=O)-(CH_2)_{2-6}-R^{12}$, and

-(CH₂)₁₋₆-NHS(=O)₂-(CH₂)₂₋₆-R¹²;

R¹⁰[[,]] and R¹³ are independently selected from the group consisting of hydrogen, linear, branched, or cyclic C₁-C₆-alkyl, alkenyl, or alkynyl; mono- or di- C₁-C₆ alkylamino, mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl-C₁-C₆-alkyl, mono- or bicyclic heteroaryl-C₁-C₆-alkyl, -(CH₂)₁₋₆-OR¹¹, -(CH₂)₁₋₆-SR¹¹, -(CH₂)₁₋₆-S(=O)-CH₂-R¹¹, -(CH₂)₁₋₆-S(=O)₂-CH₂-R¹¹, -(CH₂)₁₋₆-NR¹¹R¹¹, -(CH₂)₁₋₆-NHC(=O)R¹¹, -(CH₂)₁₋₆-NHS(=O)₂-CH₂-R¹¹, -(CH₂)₀₋₆-C(=O)-OH, -(CH₂)₀₋₆-C(=O)-OR¹¹, -(CH₂)₀₋₆-C(=O)-NH₂, -(CH₂)₀₋₆-C(=O)-NHR¹¹, -(CH₂)₀₋₆-C(=O)-N(R¹¹)₂, -(CH₂)₁₋₆-O-(CH₂)₂₋₆-R¹², -(CH₂)₁₋₆-S-(CH₂)₂₋₆-R¹², -(CH₂)₁₋₆-S(=O)-(CH₂)₂₋₆-R¹², -(CH₂)₁₋₆-S(=O)₂-(CH₂)₂₋₆-R¹², -(CH₂)₁₋₆-NH-(CH₂)₂₋₆-R¹², -(CH₂)₁₋₆-N-{(CH₂)₂₋₆-R¹²}₂, -(CH₂)₁₋₆-NHC(=O)-(CH₂)₂₋₆-R¹², and -(CH₂)₁₋₆-NHS(=O)₂-(CH₂)₂₋₆-R¹²; wherein

R¹¹ is independently selected from the group consisting of hydrogen, C₁-C₆-alkyl, alkenyl, or alkynyl; mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl-C₁-C₆-alkyl, mono- or bicyclic heteroaryl-C₁-C₆-alkyl; and

R¹² is selected from the group consisting of hydroxy, C₁-C₆-alkyloxy, aryloxy, heteroaryloxy, thio, C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, arylthio, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, amino, mono- or di-C₁-C₆-alkylamino, mono- or diarylamino, mono- or diheteroarylarnino, N-alkyl-N-arylamino, N-alkyl-N-heteroarylarnino, N-aryl-N-heteroarylarnino, aryl-C₁-C₆-alkylarnino, carboxylic acid, carboxamide, mono- or di-C₁-C₆-alkylcarboxamide, mono- or diarylcarboxamide, mono- or diheteroarylcarboxamide, N-alkyl-N-arylcarboxamide, N-alkyl-N-heteroarylcarboxamide, N-aryl-N-heteroarylcarboxamide, sulfonic acid, sulfonamide, mono- or di-C₁-C₆-alkylsulfonamide, mono- or diarylsulfonamide, mono- or diheteroarylsulfonamide, N-alkyl-N-arylsulfonamide, N-alkyl-N-heteroarylsulfonamide, N-aryl-N-heteroarylsulfonamide, urea; mono- di- or tri-substituted urea, wherein the

subsitutent(s) is selected from the group consisting of C_1 - C_6 -alkyl, aryl, heteroaryl; O-alkylurethane, O-arylurethane, and O-heteroarylurethane;

R^{14} is selected from the group consisting of hydrogen, linear, branched, or cyclic C_1 - C_6 -alkyl, alkenyl, or alkynyl; mono- or di- C_1 - C_6 alkylamino, mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl- C_1 - C_6 -alkyl, mono- or bicyclic heteroaryl- C_1 - C_6 -alkyl, $-S(=O)_2-(CH_2)_{1-6}-R^{11}$, $-C(=O)R^{11}$, $-S(=O)_2-(CH_2)_{2-6}R^{12}$, and $-C(=O)-(CH_2)_{1-6}R^{12}$; wherein R^{11} and R^{12} are as defined above;

R^{15} and R^{16} are selected from the group listed above for $[(R^9,)] R^{10}[(,)]$ and R^{13} , and are further selected from the group consisting of hydroxy, C_1 - C_6 -alkyloxy, aryloxy, heteroaryloxy, thio, C_1 - C_6 -alkylthio, C_1 - C_6 -alkylsulfinyl, C_1 - C_6 -alkylsulfonyl, arylthio, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, amino, mono- or di- C_1 - C_6 -alkylamino, mono- or diarylamino, mono- or diheteroarylarnino, N-alkyl-N-arylamino, N-alkyl-N-heteroarylarnino, N-aryl-N-heteroarylarnino, aryl- C_1 - C_6 -alkylamino, carboxylic acid, carboxamide, mono- or di- C_1 - C_6 -alkylcarboxamide, mono- or diarylcarboxamide, mono- or diheteroarylcarboxamide, N-alkyl-N-arylcboxamide, N-alkyl-N-heteroarylcarboxamide, N-aryl-N-heteroarylcarboxamide, sulfonic acid, sulfonamide, mono- or di- C_1 - C_6 -alkylsulfonamide, mono- or diarylsulfonamide, mono- or diheteroarylsulfonamide, N-alkyl-N-arylsulfonamide, N-alkyl-N-heteroarylsulfonamide, N-aryl-N-heteroarylsulfonamide, urea; mono- di- or tri-substituted urea, wherein the subsitutent(s) is selected from the group consisting of C_1 - C_6 -alkyl, aryl, heteroaryl; O-alkylurethane, O-arylurethane, and O-heteroarylurethane; ~~provided that R^{15} and R^{16} are not simultaneously hydrogen~~; and

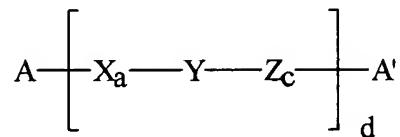
each "Y" is a single bond; and

"A" is independently selected from the group consisting of hydrogen and an amino-terminus protecting group, and "A'" is selected from the group consisting of hydroxy and a carboxy-terminus protecting group; and

each "a," "c," and "d" is an independently variable positive integer, and wherein "a" + "c" > 3;
or
salts thereof.

5. (CANCELED)

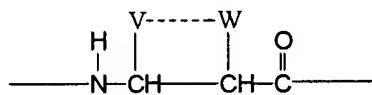
6. (CURRENTLY AMENDED) An isolated, unnatural polypeptide compound of
formula:

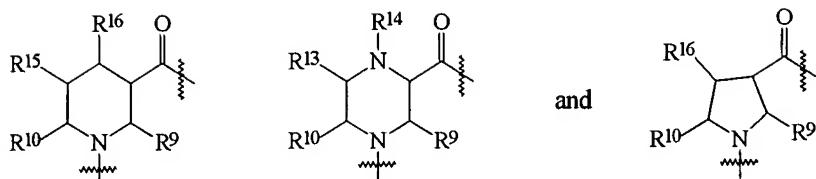
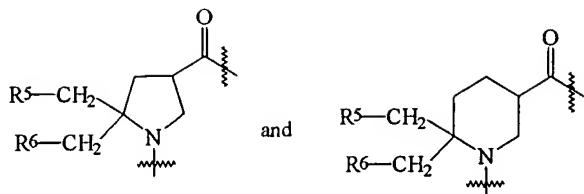


wherein:

each X and each Z is independently variable and is selected from the group consisting of α -amino acid residues, β -amino acid residues, and γ -amino acid residues, provided that at least one X or Z is an α -amino acid residue and at least another two of X or Z comprise are two cyclically-constrained residues, the two cyclically-constrained residues comprising being cyclically-constrained β -amino acid residues or cyclically-constrained γ -amino acid residues, or one cyclically-constrained β -amino acid residue and one cyclically-constrained γ -amino acid residue; and

wherein the cyclically-constrained β -amino acid residues are selected from the group consisting of:





wherein V and W are combined, together with the carbon atoms to which they are bonded, and independently define a substituted or unsubstituted, monocyclic or bicyclic C₃-C₁₀ cycloalkyl, cycloalkenyl or heterocyclic ring having one or more N, O or S atom(s) as the heteroatom(s);

the substituents on carbon atoms of the rings being independently selected from the group consisting of linear, branched, or cyclic C₁-C₆-alkyl, alkenyl, alkynyl; mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl-C₁-C₆-alkyl, and mono- or bicyclic heteroaryl-C₁-C₆-alkyl, and the substituents listed above for V and W;

the substituents on nitrogen heteroatoms of the rings being independently selected from the group consisting of hydrogen, monocyclic or bicyclic C₁-C₁₀-alkyl, alkenyl, or alkynyl; mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl-C₁-C₆-alkyl, mono- or bicyclic heteroaryl-C₁-C₆-alkyl, -S(=O)₂-R¹⁷, -C(=O)-R¹⁷, -S(=O)₂-(CH₂)_{n+1}-R¹⁸, and -C(=O)-(CH₂)_n-R¹⁸, where n = 1 to 6;

wherein R¹⁷ is independently selected from the group consisting of hydrogen, monocyclic or bicyclic C₁-C₁₀-alkyl, alkenyl, or alkynyl; mono- or bicyclic aryl, mono-

or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl-C₁-C₆-alkyl, mono- or bicyclic heteroaryl-C₁-C₆-alkyl; and

wherein R¹⁸ is independently selected from the group consisting of hydroxy, linear, branched, or cyclic C₁-C₆-alkyl, alkenyl, or alkynyl; mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl-C₁-C₆-alkyl; mono- or bicyclic heteroaryl-C₁-C₆-alkyl; C₁-C₆-alkyloxy, aryloxy, heteroaryloxy, thio, C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, arylthio, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, amino, mono- or di-C₁-C₆-alkylamino, mono- or diarylamino, mono- or diheteroaryl amino, N-alkyl-N-aryl amino, N-alkyl-N-heteroaryl amino, N-aryl-N-heteroaryl amino, aryl-C₁-C₆-alkyl amino, carboxylic acid, carboxamide, mono- or di-C₁-C₆-alkylcarboxamide, mono- or diarylcarboxamide, mono- or diheteroarylcarboxamide, N-alkyl-N-arylcarboxamide, N-alkyl-N-heteroarylcarboxamide, N-aryl-N-heteroarylcarboxamide, sulfonic acid, sulfonamide, mono- or di-C₁-C₆-alkylsulfonamide, mono- or diarylsulfonamide, mono- or diheteroarylsulfonamide, N-alkyl-N-arylsulfonamide, N-alkyl-N-heteroarylsulfonamide, N-aryl-N-heteroarylsulfonamide, urea; mono- di- or tri-substituted urea, wherein the substituent(s) is selected from the group consisting of C₁-C₆-alkyl, aryl, heteroaryl; O-alkylurethane, O-arylurethane, and O-heteroarylurethane; and

wherein R⁵ and R⁶ are independently selected from the group consisting of hydrogen, hydroxy, linear, branched, or cyclic C₁-C₁₆-alkyl, alkenyl, or alkynyl; mono- or di- C₁-C₁₆ alkylamino; mono- or bicyclic aryl; mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl-C₁-C₁₆-alkyl; mono- or bicyclic heteroaryl-C₁-C₁₆-alkyl; -(CH₂)₀₋₆-OR⁷, -(CH₂)₀₋₆-SR⁷, -(CH₂)₀₋₆-S(=O)-CH₂-R⁷, -(CH₂)₀₋₆-S(=O)₂-CH₂-R⁷, -(CH₂)₀₋₆-NR⁷R⁷, -(CH₂)₀₋₆-NHC(=O)R⁷, -(CH₂)₀₋₆-NHS(=O)₂-CH₂-R⁷, -(CH₂)₀₋₆-C(=O)-OH, -(CH₂)₀₋₆-C(=O)-OR⁷, -(CH₂)₀₋₆-C(=O)-NH₂, -(CH₂)₀₋₆-C(=O)-NHR⁷, -(CH₂)₀₋₆-C(=O)-N(R⁷)₂, -(CH₂)₀₋₆-O-(CH₂)₂₋₆-R⁸, -(CH₂)₀₋₆-S-(CH₂)₂₋₆-R⁸, -(CH₂)₀₋₆-S(=O)-(CH₂)₂₋₆-R⁸, -(CH₂)₀₋₆-S(=O)₂-(CH₂)₂₋₆-R⁸,

$-(CH_2)_{0-6}-NH-(CH_2)_{2-6}-R^8$, $-(CH_2)_{0-6}-N-\{(CH_2)_{2-6}-R^8\}_2$, $-(CH_2)_{0-6}-NHC(=O)-(CH_2)_{2-6}-R^8$, and $-(CH_2)_{0-6}-NHS(=O)_2-(CH_2)_{2-6}-R^8$; wherein

R^7 is independently selected from the group consisting of hydrogen, C_1-C_6 -alkyl, alkenyl, or alkynyl; mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl- C_1-C_6 -alkyl, mono- or bicyclic heteroaryl- C_1-C_6 -alkyl; and

R^8 is selected from the group consisting of hydroxy, C_1-C_6 -alkyloxy, aryloxy, heteroaryloxy, thio, C_1-C_6 -alkylthio, C_1-C_6 -alkylsulfinyl, C_1-C_6 -alkylsulfonyl, arylthio, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, amino, mono- or di- C_1-C_6 -alkylamino, mono- or diarylamino, mono- or diheteroaryl amino, N-alkyl-N-arylamino, N-alkyl-N-heteroaryl amino, N-aryl-N-heteroaryl amino, aryl- C_1-C_6 -alkylamino, carboxylic acid, carboxamide, mono- or di- C_1-C_6 -alkylcarboxamide, mono- or diarylcarboxamide, mono- or diheteroarylcarboxamide, N-alkyl-N-arylcarboxamide, N-alkyl-N-heteroarylcarboxamide, N-aryl-N-heteroarylcarboxamide, sulfonic acid, sulfonamide, mono- or di- C_1-C_6 -alkylsulfonamide, mono- or diarylsulfonamide, mono- or diheteroarylsulfonamide, N-alkyl-N-arylsulfonamide, N-alkyl-N-heteroarylsulfonamide, N-aryl-N-heteroarylsulfonamide, urea; mono- di- or tri-substituted urea, wherein the substituent(s) is selected from the group consisting of C_1-C_6 -alkyl, aryl, heteroaryl; O-alkylurethane, O-arylurethane, and O-heteroarylurethane;

wherein $R^9[[,]]$ is selected from the group consisting of linear, branched, or cyclic C_1-C_6 -alkyl, alkenyl, or alkynyl; mono- or di- C_1-C_6 alkylamino, mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl- C_1-C_6 -alkyl, mono- or bicyclic heteroaryl- C_1-C_6 -alkyl, $-(CH_2)_{1-6}-OR^{11}$, $-(CH_2)_{1-6}-SR^{11}$, $-(CH_2)_{1-6}-S(=O)-CH_2-R^{11}$, $-(CH_2)_{1-6}-S(=O)_2-CH_2-R^{11}$, $-(CH_2)_{1-6}-NR^{11}R^{11}$, $-(CH_2)_{1-6}-NHC(=O)R^{11}$, $-(CH_2)_{1-6}-NHS(=O)_2-CH_2-R^{11}$, $-(CH_2)_{0-6}-C(=O)-OH$, $-(CH_2)_{0-6}-C(=O)-OR^{11}$, $-(CH_2)_{0-6}-C(=O)-NH_2$, $-(CH_2)_{0-6}-C(=O)-NHR^{11}$, $-(CH_2)_{0-6}-C(=O)-N(R^{11})_2$, $-(CH_2)_{1-6}-O-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-S-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-S(=O)-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-S(=O)_2-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-NH-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-N-\{(CH_2)_{2-6}-R^{12}\}_2$, $-(CH_2)_{1-6}-NHC(=O)-(CH_2)_{2-6}-R^{12}$, and $-(CH_2)_{1-6}-NHS(=O)_2-(CH_2)_{2-6}-R^{12}$; and

$R^{10}[[,]]$ and R^{13} are independently selected from the group consisting of hydrogen, linear, branched, or cyclic C_1-C_6 -alkyl, alkenyl, or alkynyl; mono- or di- C_1-C_6 alkylamino, mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl- C_1-C_6 -alkyl, mono- or bicyclic heteroaryl- C_1-C_6 -alkyl, $-(CH_2)_{1-6}-OR^{11}$, $-(CH_2)_{1-6}-SR^{11}$, $-(CH_2)_{1-6}-S(=O)-CH_2-R^{11}$, $-(CH_2)_{1-6}-S(=O)_2-CH_2-R^{11}$, $-(CH_2)_{1-6}-NR^{11}R^{11}$, $-(CH_2)_{1-6}-NHC(=O)R^{11}$, $-(CH_2)_{1-6}-NHS(=O)_2-CH_2-R^{11}$, $-(CH_2)_{0-6}-C(=O)-OH$, $-(CH_2)_{0-6}-C(=O)-OR^{11}$, $-(CH_2)_{0-6}-C(=O)-NH_2$, $-(CH_2)_{0-6}-C(=O)-NHR^{11}$, $-(CH_2)_{0-6}-C(=O)-N(R^{11})_2$, $-(CH_2)_{1-6}-O-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-S-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-S(=O)-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-S(=O)_2-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-NH-(CH_2)_{2-6}-R^{12}$, $-(CH_2)_{1-6}-N-\{(CH_2)_{2-6}-R^{12}\}_2$, $-(CH_2)_{1-6}-NHC(=O)-(CH_2)_{2-6}-R^{12}$, and $-(CH_2)_{1-6}-NHS(=O)_2-(CH_2)_{2-6}-R^{12}$, wherein

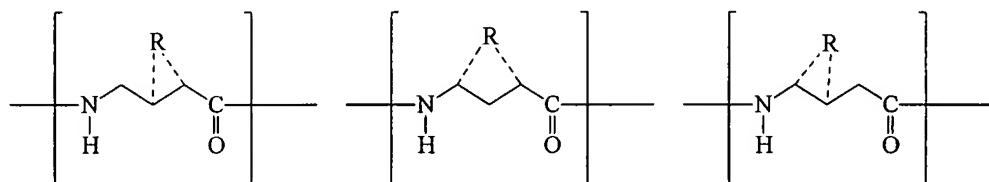
R^{11} is independently selected from the group consisting of hydrogen, C_1-C_6 -alkyl, alkenyl, or alkynyl; mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl- C_1-C_6 -alkyl, mono- or bicyclic heteroaryl- C_1-C_6 -alkyl; and

R^{12} is selected from the group consisting of hydroxy, C_1-C_6 -alkyloxy, aryloxy, heteroaryloxy, thio, C_1-C_6 -alkylthio, C_1-C_6 -alkylsulfinyl, C_1-C_6 -alkylsulfonyl, arylthio, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, amino, mono- or di- C_1-C_6 -alkylamino, mono- or diarylamino, mono- or diheteroaryl amino, N-alkyl-N-arylamino, N-alkyl-N-heteroaryl amino, N-aryl-N-heteroaryl amino, aryl- C_1-C_6 -alkylamino, carboxylic acid, carboxamide, mono- or di- C_1-C_6 -alkylcarboxamide, mono- or diarylcarboxamide, mono- or diheteroarylcarboxamide, N-alkyl-N-arylcarboxamide, N-alkyl-N-heteroarylcarboxamide, N-aryl-N-heteroarylcarboxamide, sulfonic acid, sulfonamide, mono- or di- C_1-C_6 -alkylsulfonamide, mono- or diarylsulfonamide, mono- or diheteroarylsulfonamide, N-alkyl-N-arylsulfonamide, N-alkyl-N-heteroarylsulfonamide, N-aryl-N-heteroarylsulfonamide, urea; mono- di- or tri-substituted urea, wherein the substituent(s) is selected from the group consisting of C_1-C_6 -alkyl, aryl, heteroaryl; O-alkylurethane, O-arylkurethane, and O-heteroarylkurethane;

R^{14} is selected from the group consisting of hydrogen, linear, branched, or cyclic C_1 - C_6 -alkyl, alkenyl, or alkynyl; mono- or di- C_1 - C_6 alkylamino, mono- or bicyclic aryl, mono- or bicyclic heteroaryl having up to 5 heteroatoms selected from N, O, and S; mono- or bicyclic aryl- C_1 - C_6 -alkyl, mono- or bicyclic heteroaryl- C_1 - C_6 -alkyl, $-S(=O)_2-(CH_2)_{1-6}R^{11}$, $-C(=O)R^{11}$, $-S(=O)_2-(CH_2)_{2-6}R^{12}$, and $-C(=O)-(CH_2)_{1-6}R^{12}$; wherein R^{11} and R^{12} are as defined above;

R^{15} and R^{16} are selected from the group listed above for $[[R^9,]] R^{10}[[,]]$ and R^{13} , and are further selected from the group consisting of hydroxy, C_1 - C_6 -alkyloxy, aryloxy, heteroaryloxy, thio, C_1 - C_6 -alkylthio, C_1 - C_6 -alkylsulfinyl, C_1 - C_6 -alkylsulfonyl, arylthio, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, amino, mono- or di- C_1 - C_6 -alkylamino, mono- or diarylamino, mono- or diheteroaryl amino, N-alkyl-N-arylamino, N-alkyl-N-heteroaryl amino, N-aryl-N-heteroaryl amino, aryl- C_1 - C_6 -alkylamino, carboxylic acid, carboxamide, mono- or di- C_1 - C_6 -alkylcarboxamide, mono- or diarylcarboxamide, mono- or diheteroarylcarboxamide, N-alkyl-N-arylcarboxamide, N-alkyl-N-heteroarylcarboxamide, N-aryl-N-heteroarylcarboxamide, sulfonic acid, sulfonamide, mono- or di- C_1 - C_6 -alkylsulfonamide, mono- or diarylsulfonamide, mono- or diheteroarylsulfonamide, N-alkyl-N-arylsulfonamide, N-alkyl-N-heteroarylsulfonamide, N-aryl-N-heteroarylsulfonamide, urea; mono- di- or tri-substituted urea, wherein the substituent(s) is selected from the group consisting of C_1 - C_6 -alkyl, aryl, heteroaryl; O-alkylurethane, O-arylurethane, and O-heteroarylurethane, **provided that R^{15} and R^{16} are not simultaneously hydrogen**; and

wherein the cyclically-constrained γ -amino acid residues are selected from the group consisting of:



wherein R, together with the carbons to which it is attached, and further together with the β -position carbon in the γ -amino acid backbone where appropriate, independently defines a substituted or unsubstituted, monocyclic or bicyclic C₃ to C₁₀ cycloalkyl, cycloalkenyl, or heterocycle moiety, the heterocycle moiety having 1, 2, or 3 heteroatoms selected from the group consisting of N, S, and O; and

each "Y" is a single bond; and

"A" is independently selected from the group consisting of hydrogen and an amino-terminus protecting group, and "A'" is selected from the group consisting of hydroxy and a carboxy-terminus protecting group; and

each "a," "c," and "d" is an independently variable positive integer, and wherein "a" + "c" > 3; or

salts thereof.

7. (CANCELED)

8. (ORIGINAL) The compound of Claim 6, wherein at least one of X or Z is a cyclically-constrained β -amino acid residue wherein V and W, and the carbon atoms to which they are bonded, define a substituted or unsubstituted C₄ to C₆ cycloalkyl, cycloalkenyl, or heterocyclic ring having one nitrogen atom as the sole heteroatom.

9. (ORIGINAL) The compound of Claim 6, wherein at least one of X or Z is a cyclically-constrained β -amino acid residue wherein V and W, and the carbon atoms to which they are bonded, define a substituted or unsubstituted cyclopentyl, cyclohexyl, pyrrolidinyl, or piperdinyl ring.

10. (CANCELED)

11. (WITHDRAWN and PREVIOUSLY PRESENTED) A method of probing, disrupting, or mimicking binding interactions between two protein molecules or fragments thereof, the method comprising:

in an *in vivo*, *in vitro*, or *ex vivo* reaction between the two proteins,

- (a) introducing to the reaction an unnatural polypeptide compound according to Claim 4; and then
- (b) quantifying any effect of the added compound from step (a) on thermodynamic or kinetic parameters of the binding interaction between the two protein molecules or fragments thereof.

12-14. (CANCELED)